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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,506	11/13/2003	Sanjay Awasthi	124263-1007	1056

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/714,506	AWASTHI ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11 and 19-20, as specifically drawn to a method of treating cells undergoing uncontrolled growth comprising contacting the cells with an antibody to RLIP76, classified in class 424, subclass 130.1.

II. Claims 12-18, as specifically drawn to a pharmaceutical composition comprising an antibody to RLIP76, classified in class 530, subclass 387.1.

The inventions are distinct, each from the other because of the following reasons:

The inventions of Group II and Group I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process such as affinity chromatography.

Because the inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search required for each group is not required for other groups because each group requires a different non-patent literature search due to each group comprising different products and/or method steps, restriction for examination purposes as indicated is proper.

Species Election

This application contains claims directed to the following patentably distinct species of the claimed invention:

Claim 2 (Group I) is generic to a plurality of disclosed patentably distinct species comprising the following cancerous cells: NCI-H82, NCI-H182, NCI-1417 ... HCC$$ (adenocarcinoma), and NCI-H2126 (large cell) which differ at least in morphologies and functions such that one species could not be interchanged with the other. As such, each species would require different searches and the consideration of different patentability issues.

Claim 7 (Group I) is generic to a plurality of disclosed patentably distinct species comprising the following drugs: doxorubicin, actinomycin, actinomycin D, altreatamine ... vincristine, vindesine, and vinorelbine which differ at least in chemical structure and mechanism of action such that one species could not be interchanged with the other. As such, each species would require different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone conversation with Thomas Wright a provisional election was made without traverse to prosecute the invention of Group I, claims 1-11 and 19-20. Applicants further elected the following cancer cell from claim 2, HCI-H2126, and the following drug from claim 7, doxorubicin, as the species. After reconsideration, the species elections have been withdrawn by the Examiner. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 1-20 are pending.

Claims 12-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-11 and 19-20 are currently under consideration.

Claim Objections

Claim 20 is objected to because of the following informalities: In the instant case, Claim 20 is drawn to the method of claim 17, but claim 17 is a product and not a method. For examination purposes, Claim 20 will be interpreted as being dependent from the method of claim 19.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 19-22 are rejected as vague and indefinite for reciting the term RLIP76 as the sole means of identifying the claimed molecule. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify RLIP76, for example, by SEQ ID NO. and function of RLIP76. For example, a search of iHop database reveals RLIP76 is known by other laboratories as 76-kDa RaI-interacting protein, Dinitrophenyl S-glutathione ATPase, DNP-SG ATPase, raIA binding protein 1, RaIBP1, RaI interacting protein 1, RIP, RIP1 and RLIP1 (see attached). Thus, it does not appear that the term "RLIP76" is the standard throughout all laboratories.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2002; 43: Abst.).

Awasthi *et al.* teaches a method of treating 6 NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with polyclonal RLIP76 antibodies, wherein the administration of the antibodies results in apoptosis. Moreover, the reference discloses that the method further comprises administering a drug used in chemotherapy, e.g., doxorubicin, in combination with the antibody, wherein the addition of the drug to the antibody enhanced the cytotoxicity of the drug. In addition to doxorubicin, Awasthi *et al.* also teach that the combination of Herceptin and anti-RLIP76 resulted in an additive effect with regards to cytotoxicity. Although Awasthi et al does not specifically teach that the antibody to RLIP76 inhibits the transport activity of RLIP76 resulting in the prevention of a drug from leaving the cell, the claimed functional limitation would be an inherent property of the referenced method because as evidenced by Sharma *et al.* (Arch. Biochem. Biophys. 2001; 391: 171-179) ATP dependent inhibition of the ATP-dependent transport of DOX was inhibited in erythrocyte inside-out vesicles coated with antibodies against RLIP76 (Abstract). Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1 and 3-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst.).

Awasthi *et al.* teaches a method of treating both SCLC and NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with anti-RLIP76 antibodies which recognize a cell surface epitope in lung cancer cells. The reference further teaches that the administration of anti-RLIP76 to the cells resulted in DNA laddering demonstrating apoptotic activity. Moreover,

Awasthi *et al.* discloses that the method further comprises administering a drug used in chemotherapy, e.g., doxorubicin, in combination with the antibody, wherein the addition of the drug to the antibody enhanced the cytotoxicity of the drug. Although Awasthi *et al.* does not specifically teach that the antibody to RLIP76 inhibits the transport activity of RLIP76 resulting in the prevention of a drug from leaving the cell, the claimed functional limitation would be an inherent property of the referenced method because as evidenced by Sharma *et al.* (Arch. Biochem. Biophys. 2001; 391: 171-179) ATP dependent inhibition of the ATP-dependent transport of DOX was inhibited in erythrocyte inside-out vesicles coated with antibodies against RLIP76 (Abstract). Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst.) in combination with American Type Culture Collection (Tumor Cell Lines, 2001).

Awasthi *et al.* teaches a method of treating both SCLC and NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with anti-RLIP76 antibodies which recognize a cell surface epitope in lung cancer cells.

Awasthi *et al.* does not teach that the cells are selected from the group of cancerous cells consisting of NCI-H82, NCI-H182, NCI-1417, NCI-1618, NCI-H1395, NCI-H2347, HCC44 (adenocarcinoma), and NCI-H2126.

American Type Culture Collection discloses a plethora of commercially available tumor cell lines including but not limited cell lines obtained from SCLC and NSCLC such as NCI-H82, NCI-1417, NCI-1618, NCI-H1395, NCI-H2341 and NCI-H2126.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a SCLC or NSCLC tumor cell line in the method of Awasthi *et al.*. One would have been motivated to do so because the American Type Culture Collection discloses commercially available lung tumor cell lines, SCLC and NSCLC, while Awasthi *et al.* teaches a method of treating SCLC and NSCLC cell lines undergoing uncontrolled cell growth with RLIP76 antibodies which specifically recognize an epitope in lung cancer cells. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by combining a SCLC or NSCLC tumor cell line available through ATCC with the method as taught by Awasthi et al., one would achieve a method of treating uncontrolled cell growth in at least NCI-H82, NCI-1417, NCI-1618, NCI-H1395, NCI-H2341 and NCI-H2126 cells.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst.) in view of Sause WT (Chest, 1999; 116: 504S-508S).

Awasthi *et al.* teaches a method of treating both SCLC and NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with RLIP76 antibodies which recognize a cell surface epitope in lung cancer cells, wherein ant-RLIP76 promotes apoptosis in the cell.

Awasthi *et al.* does not teach that the antibody is added in combination with radiation therapy.

Sause teaches the role of radiotherapy in non-small cell lung cancer. Specifically, the reference teaches that radiation therapy (RT) is an effective method of local disease control for non-

small lung cancer (NSCLC) and can be used for definitive management in selected patients (page 504S, 1st column, 1st paragraph).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to treat one or more cells undergoing uncontrolled growth. One of skill in the art would have been motivated to so because each of the therapeutics had been individually taught in the prior art to be successful at treating cells undergoing uncontrolled growth such as cancer. The instant situation is amenable to the type of analysis set forth in In re Kerkhoven,205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant method claims, one of ordinary skill in the art would have reasonably expected that by adding RLIP76 antibodes in combination with radiation therapy, one would achieve an enhanced method of treating cell undergoing uncontrolled growth.

Moreover, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983).

Claims 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen *et al.* (US 2002/0119156, 2001) in combination with Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst.).

Chen *et al.* teaches (abstract) antibodies immunospecific for polypeptides expressed in lung cancer, as well as methods for detecting, diagnosing, monitoring, staging and imaging lung cancer, i.e., cells undergoing uncontrolled growth. The publication further teaches (page 2, paragraph 0022) that the antibodies can be labeled with a variety of detectable labels including, not limited to, radioisotopes and paramagnetic metals. For example, Chen *et al.* discloses (page 13, paragraph 0154) that the labeled immunospecific antibodies can be injected into patients suspected of having lung cancer for the purposes of diagnosing and/or staging the disease status of the patient, wherein the

amount of label within an organ or tissue allows for the determination of the presence or absence of cancer in that organ or tissue.

Chen *et al.* does not teach that the antibody is specific for RLIP76.

Awasthi *et al.* teaches an antibody to RLIP76, which specifically recognizes a cell surface epitope in lung cancers.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to label an antibody to RLIP76 as taught by Awasthi *et al.* for the purposes of identifying a cell undergoing uncontrolled growth as taught by Chen *et al.*. One would have been motivated to do so because Awasthi *et al.* provides antibodies which specifically recognizes a cell surface epitope, RLIP76, in lung cancer cells. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by combing anti-RLIP as taught by Awasthi et al. with the method taught by Chen et al., one would achieve a method of determining the presence or absence of lung cancer.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
6/22/05